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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/623,802	07/22/2003	Martin C. M. M. Barnardo	1181-282	5302

6449 7590 10/21/2005

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EXAMINER	
COUNTS, GARY W	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 10/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/623,802	BARNARDO ET AL.	
	Examiner	Art Unit	
	Gary W. Counts	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/3/04,& 07/15/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Sequence Compliance

(1) The application clearly fails to comply with the requirement of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

(2) This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

(3) A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

Applicant must provide:

An initial or substitute computer readable from (CFR) copy of the "Sequence Listing".

An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

A statement that the content of the paper and computer readable copies are the same and, where applicable, include not new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or1.825(d).

A statement to request transfer of sequences from application 09/809,029 to 10/623,802. (see sample statement attached).

The time for reply of the sequence compliance is set to the time of reply for the office action.

Specification

1. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. See for example, page 10 of the specification.

2. The disclosure is objected to because of the following informalities: the disclosure does not provide a section briefly describing the drawings.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. On page 9, lines 15-23 in the specification. The applicant discloses functionally equivalent variants, derivatives or fragments refer to MHC molecules related to or derived from naturally occurring MHC molecules wherein the amino acid sequence of one or more components of said MHC molecules (e.g. the class I heavy chain, class II) has been modified by single or multiple amino acid (e.g. at 1 to 50, e.g. 10 to 30, preferably 1 to 5 bases) substitution, addition and/or deletion but which nonetheless retains functional activity. On page 10, lines 7-13 in the specification. The applicant discloses that the derivatives and variants are closely related to one or more components of the naturally occurring MHC molecules, e.g. are encoded by nucleic acid molecules with more that 70%, preferably more than 80, 90 or 95% sequence identity to naturally occurring sequences or exhibit such sequence

identity to the functional portions of these sequences. Further, on page 11, line 27-page 12, line 3 the applicant discloses the fragments may be derived from naturally occurring molecules or from functionally equivalent variants or derivatives thereof. Preferably the fragments are between 50 and 500 residues, e.g. 100 and 250 residues in length. The applicant does not disclose all recombinant MHC molecules or functionally equivalent recombinant variants, derivatives or fragments thereof. Further, the applicant does not disclose the nucleic acid sequence encoding the variants, which is required. Furthermore, in *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA... 'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere which or plan for obtaining the claimed chemical invention".

Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid sequence encoding the variants is required. See *Fiers v. Revel,* 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.,* 18 USPQ2d 1016.

5. Claims 1-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for recombinant MHC monomers, known allelic variants and specific peptides, does not reasonably provide enablement for all recombinant MHC molecules or functionally equivalent recombinant variants, derivative or fragments thereof.. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. The factors that must be considered in determining undue experimentation are set forth in *In re W*ands USPTQ2d 14000. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The instant claims are directed to a method of depleting a sample of MHC molecule antibodies comprising at least the steps of contacting said sample with one or more recombinant MHC molecules or functionally equivalent variants, derivative or fragments thereof, optionally attached to a solid support and removing at least the recombinant MHC molecules to which antibodies contained within the sample have bound. The specification on page 5, lines 9-10 and page 17 discloses recombinant MHC monomers. The applicant discloses functionally equivalent variants, derivatives or fragments refer to MHC molecules

related to or derived from naturally occurring MHC molecules wherein the amino acid sequence of one or more components of said MHC molecules (e.g. the class I heavy chain, class II) has been modified by single or multiple amino acid (e.g. at 1 to 50, e.g. 10 to 30, preferably 1 to 5 bases) substitution, addition and/or deletion but which nonetheless retains functional activity. On page 10, lines 7-13 in the specification. The applicant discloses that the derivatives and variants are closely related to one or more components of the naturally occurring MHC molecules, e.g. are encoded by nucleic acid molecules with more that 70%, preferably more than 80, 90 or 95% sequence identity to naturally occurring sequences or exhibit such sequence identity to the functional portions of these sequences. Further, on page 11, line 27 – page 12, line 3 the applicant discloses the fragments may be derived from naturally occurring molecules or from functionally equivalent variants or derivatives thereof. Preferably the fragments are between 50 and 500 residues, e.g. 100 and 250 residues in length. The applicant does not disclose all recombinant MHC molecules or functionally equivalent recombinant variants, derivatives or fragments thereof to detect anti MHC or anti HLA antibodies. It is possible the combinations of variants, derivatives or fragments thereof may lose their functionality and thus would not work to detect the antibodies.

The working examples in the specification are directed to recombinant monomers HLA-A2 and HLA-B8. At best, the detection of the HLA antibodies can be determined only by using recombinant monomers or known allelic variants. There is no guidance in the specification disclosing which derivatives, variants, fragments or combinations thereof, which can be used for the depletion of MHC molecule antibodies. Such is not seen as sufficient to support the breath of the claims and one skilled in the art cannot practice the claimed invention without

undue experimentation, because in order to deplete the anti-MHC antibodies one skilled in the art would have to perform experiments to determine which variants, derivatives or fragments did or did not function to bind to the anti-MHC antibodies.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite because of the use of an acronym: i.e. MHC. Although the term may have art recognized meanings, it is unclear if applicant intends to claim the prior art definitions. The term should be defined in its first instance.

Claim 1 is vague and indefinite because the preamble of the claim does not correlate with the body of the claim. The preamble of the claim recites a method of depleting a sample of MHC molecule antibodies. However, the body of the claim does not positively recite the depletion of antibodies from the sample. The claim merely requires contacting a sample with a recombinant MHC molecule.

Claim 1, lines 3 and 4 the recitation "functionally equivalent variants" is vague and indefinite. There is no definition provided in the specification for this term and it is unclear what applicant intends. See also deficiency found in claim 19.

Claim 1, line 7 the recitation "have bound" there is insufficient antecedent basis for this limitation. It appears that the claim lacks a step of binding the MHC molecule to the antibody.

Claim 3 and 4 the recitation "said hla molecule" as depending upon claim 1. There is insufficient antecedent basis for this limitation.

Claim 5 the recitation "the heavy chain" there is insufficient antecedent basis for this limitation.

Claim 8 "a variant" is vague and indefinite. There is no definition provided in the specification for the term and it is unclear what applicant is trying to encompass. Please clarify.

Claim 21 "a variant" is vague and indefinite. There is no definition provided in the specification for the term and it is unclear what applicant is trying to encompass. Please clarify.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1-7, 13 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Walter et al., (Stimulation of human cytotoxic T cells with HIV-1derived peptides presented by recombinant HLA-A2 peptide complexes, International Immunology, vol. 9, No. 3, pp. 451-459, 1997).

Walter et al., disclose contacting a recombinant HLA-A2 peptide complex with a sample comprising W6/32 antibodies which bind to the recombinant HLA.

With respect to the depleting of antibodies as recited in the instant claims. By way of applicant's statement on page 21, lines 1-5 of the specification which states "It will be understood that contacting a sample with recombinant MHC molecule will remove antibodies which bind to the MHC molecule" and since Walter et al teaches contacting a recombinant MHC molecule with antibodies of a sample, Walter et al teaches depleting of antibodies. Further, the body of the claim does not require the depleting of antibodies. It is also noted that since the claim recites "optionally" in line 4 of claim 1, all the following recitations after the recitation of "optionally" are not required. Therefore, for the reasons stated above Walter et al reads on the instantly recited claims.

10. Claims 1-8, and 17 are rejected under 35 U.S.C. 102(a) as being anticipated by Barnardo et al (Detection of HLA antibodies using single recombinant HLA alleles, Human Immunology, Abstracts 1999, Volume 60, Supplement 2).

Barnardo et al., disclose contacting a recombinant HLA-A2 with a sample comprising HLA antibodies which bind to the recombinant HLA. Barnardo et al disclose that the HLA is biotinylated.

With respect to the depleting of antibodies as recited in the instant claims. By way of applicant's statement on page 21, lines 1-5 of the specification which states "It will be understood that contacting a sample with recombinant MHC molecule will remove antibodies which bind to the MHC molecule" and since Barnardo et al teaches

contacting a recombinant MHC molecule with antibodies of a sample, Barnardo et al teaches depleting of antibodies. Further, the body of the claim does not require the depleting of antibodies. It is also noted that since the claim recites "optionally" in line 4 of claim 1, all the following recitations after the recitation of "optionally" are not required. Therefore, for the reasons stated above Walter et al reads on the instantly recited claims.

It is noted that the above reference Barnardo et al has common authors which are listed as inventors in the current application. It is also noted that the above reference is considered prior art because it is considered to be by others, because the reference lists Olivia Shaw and Graham Ogg as authors and Shaw and Ogg are not listed as inventors of the current application. Therefore, it is considered to be by others.

11. Claims 1-8, and 17 are rejected under 35 U.S.C. 102(a) as being anticipated by Barnardo et al (Detection of HLA-Specific IgG using single, recombinant HLA alleles, Human Immunology (1999) Vol 60., No. Suppl. 1, pp. S1.

Barnardo et al., disclose contacting a recombinant HLA-A2 with a sample comprising HLA antibodies which bind to the recombinant HLA. Barnardo et al disclose that the HLA is biotinylated.

With respect to the depleting of antibodies as recited in the instant claims. By way of applicant's statement on page 21, lines 1-5 of the specification which states "It will be understood that contacting a sample with recombinant MHC molecule will remove antibodies which bind to the MHC molecule" and since Barnardo et al teaches contacting a recombinant MHC molecule with antibodies of a sample, Barnardo et al

teaches depleting of antibodies. Further, the body of the claim does not require the depleting of antibodies. It is also noted that since the claim recites "optionally" in line 4 of claim 1, all the following recitations after the recitation of "optionally" are not required. Therefore, for the reasons stated above Walter et al reads on the instantly recited claims.

It is noted that the above reference Barnardo et al has common authors which are listed as inventors in the current application. It is also noted that the above reference is considered prior art because it is considered to be by others, because the reference lists Graham Ogg as an author Ogg is not listed as an inventor of the current application. Therefore, it is considered to be by others.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

14. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

15. Claims 1-7, 9, 13, 14 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Whitehead et al (US 4,554,088) in view of Walter et al (Stimulation of human cytotoxic T cells with HIV-1derived peptides presented by recombinant HLA-A2 peptide complexes, International Immunology, vol. 9, No. 3, pp. 451-459, 1997).

Whitehead et al disclose methods for depleting a sample of a biological molecule of interest by contacting the sample with an immobilized bioaffinity adsorbent. Whitehead et al disclose that the bioaffinity adsorbent can be any biological or other molecule capable of specific or nonspecific binding or interaction with another biological molecule such as antibody/antigen (col 7, lines 25-36). Whitehead et al disclose that the analyte can be immobilized to a magnetic particle. (col 6).

Whitehead et al differ from the instant invention in failing to specifically teach depleting the sample of MHC molecule antibodies.

Walter et al disclose bioaffinity adsorbents which interact with each other. Walter et al disclose that the bioaffinity adsorbents can be recombinant HLA-A2 peptides

(recombinant MHC molecule) (antigens) and W6/32 antibodies (MHC antibodies). Walter et al disclose that the HLA-A2 molecule is produced in E.Coli (prokaryotic expression system)(p.451).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate recombinant HLA-A2 peptides as the antigen into the method of Whitehead et al because Whitehead et al is generic with respect to the biological molecule to be depleted and one would use the appropriate bioaffinity reagent, i.e. recombinant HLA-A2 peptides to deplete the desired biomolecule of interest, in this case MHC molecule antibodies.

16. Claims 10-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Whitehead et al and Walter et al in view of Luxembourg et al (2004/0137617).

See above for the teachings of Whitehead et al and Walter et al.

Whitehead et al and Walter et al differ from the instant invention in failing to teach the solid support is nitrocellulose or nylon.

Luxembourg et al teaches the equivalence of a magnetic particle to nitrocellulose or nylon as a support for separation procedures (page 3).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate nitrocellulose or nylon as a support such as taught by Luxembourg et al because Luxembourg et al teaches the equivalence of nitrocellulose and nylon as solid supports for separation processes and the selection of this known equivalent to replace the solid support of Whitehead would be within the level of ordinary skill in the art.

17. Claims 8 and 18-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Whitehead et al and Walter et al in view of Tan et al (A novel, highly efficient peptide-HLA class I binding assay using unfolded heavy chain molecules, Journal of Immunological Methods 205 (2) (1997) 201-209).

See above for the teachings of Whitehead et al and Walter et al.

Whitehead et al and Walter et al differ from the instant invention in failing to specifically teach the heavy chain is recombinant.

Tan et al disclose recombinant HLA heavy chain molecules, β_2-microglobulin and a peptide (abstract). Tan et al disclose that the heavy chain is immobilized to a surface (p. 207, col 2, lines 1-2). Tan et al also disclose that an advantage of the use of this heavy chain is the improved economy and efficiency, as unfolded protein material is in principle easily accessible by recombinant technology.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate recombinant HLA heavy chain molecules as taught by Tan et al into the modified method of Whitehead et al because Tan et al shows that the use of this heavy chain is the improved economy and efficiency, as unfolded protein material is in principle easily accessible by recombinant technology.

With respect to the recitation "a variant" as recited in the instant claims. It is unclear what applicant intends and is trying to encompass (see 112 second rejections above) and since the combination of Whitehead, Walter and Tan et al disclose immobilized recombinant HLA molecules, the combined references read on the instantly recited claims.

18. Claims 15 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Whitehead et al and Walter et al in view of Burrows et al (US 2005/0074853).

See above for the teachings of Whitehead et al and Walter et al.

Whitehead et al and Walter et al differ from the instant invention in failing to teach the recombinant MHC or HLA is synthesized in a eukaryotic expression system.

Burrows et al teaches that eukaryotic systems are known for the expression of MHC polypeptides and teaches the equivalence of using E-Coli (prokaryotic, same as taught by Walter) or eukaryotic expressions systems (p. 8, col 2 – page 9, col. 1).

It would have been obvious to one or ordinary skill in the art at the time the invention was made to synthesize the recombinant molecules of Walter et al with eukaryotic expression systems because Burrows et al shows that MHC molecules can be synthesized by eukaryotic expressions systems and shows that eukaryotic systems are equivalent to prokaryotic systems. Therefore, one of ordinary skill in the art would have a reasonable expectation of success synthesizing the recombinant molecule by eukaryotic expressions system.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 2720817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary Counts
Examiner
Art Unit 1641
September 26, 2005

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600
10/14/05

Notice to Comply	Application No. 10/623,802	Applicant(s) Barnardo et al.	
	Examiner G. Counts	Art Unit 1641	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set in the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☒ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☒ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: a statement to request transfer of sequences

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", **as well as an amendment specifically directing its entry into the application**.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (571) 272-2510
For CRF Submission Help, call (571) 272-2501/2583.
PatentIn Software Program Support
Technical Assistance.....703-287-0200
To Purchase PatentIn Software.....703-306-2600

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR REPLY

V. Sample statement to request transfer of sequences

The following paragraph, or language having the same effect, can be used to invoke the procedures of 37 CFR section 1.821(e) in which an identical computer readable form from another application is used in a given application. The paragraph should be incorporated into a separate paper to be submitted in the given application.

> The computer readable form in this application, 08/100,000, is identical with that filed in Application Number 07/999,999, filed March 1, 1998. In accordance with 37 CFR 1.821(e), please use the [first-filed, last-filed or only, whichever is applicable] computer readable form filed in that application as the computer readable form for the instant application. It is understood that the Patent and Trademark Office will make the necessary change in application number and filing date for the computer readable form that will be used for the instant application. A paper copy of the Sequence Listing is [included in the originally-filed specification of the instant application, included in a separately filed preliminary amendment for incorporation into the specification whichever is applicable].

HOW TO SEND SEUQUENCES TO USPTO

The addresses below are effective 5 June 2004. Please direct all replies to the United States Patent and Trademark Office via one (1) of the following:

1. Electronically submitted through EFS-Bio (<http://www.uspto.gov/ebc/efs/downloads/documents.htm>, EFS Submission User Manual - ePAVE)

2. Mailed to:
   Mail Stop Sequence
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   P.O. Box 22313-1450
   Alexandria, VA 22313-1450

3. Hand Carry, Federal Express, United Parcel Service or other delivery service to:
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